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Proposed Registration Decision PRD2018-12

# *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01

*(publié aussi en français)*

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# Overview

## Proposed Registration Decision for *Pepino Mosaic Virus*, strain CH2, isolate 1906 and PMV-01

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing registration for the sale and use of *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01, containing the technical grade active ingredient *Pepino mosaic virus*, strain CH2, isolate 1906, to protect greenhouse tomatoes against *Pepino mosaic virus* (PepMV).

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01.

## What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides section of Canada.ca.

Before making a final registration decision on *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on *Pepino mosaic*

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

*virus*, strain CH2, isolate 1906 and PMV-01, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

## What Is *Pepino Mosaic Virus*, strain CH2, isolate 1906?

*Pepino mosaic virus* strain CH2, isolate 1906, is a mild form of the *Pepino mosaic virus* (PepMV). It protects greenhouse tomatoes against aggressive forms of the virus through cross-protection, which is a plant defense mechanism against viral infection.

## Health Considerations

### Can Approved Uses of *Pepino mosaic virus*, strain CH2, isolate 1906 Affect Human Health?

***Pepino mosaic virus*, strain CH2, isolate 1906 is unlikely to affect your health when PMV-01 is used according to the label directions.**

Potential exposure to *Pepino mosaic virus*, strain CH2, isolate 1906 may occur when handling and applying PMV-01 and ingesting treated produce. When assessing health risks, several key factors are considered:

- the microorganism's biological properties (for example, infection cycle);
- reports of any adverse incidents;
- its potential to cause disease or toxicity as determined in toxicological studies; and
- the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this microorganism.

The levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses that are determined as having no health risks of concern are considered acceptable for registration.

Studies in laboratory animals describe potential health effects from large doses of exposure to a microorganism and identify any pathogenicity, infectivity and toxicity concerns. When *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) was tested on laboratory animals, there was no sign that it caused any toxicity following oral, pulmonary or dermal exposures. Similarly, no signs of infection were observed when *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) was tested on a human cell culture. *Pepino mosaic virus* is a plant virus. Plant viruses are not related to any animal or human

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[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

pathogen. There are no reports of adverse effects despite the natural occurrence and prevalence of plant viruses in the environment and due to the limited host range.

**Residues in Water and Food**

**Dietary risks from food and water are not of concern**

The health risk to the general population, including infants and children, as a result of dietary exposure (food and drinking water), is not expected based on the use pattern and conditions of use.

**Risks in Residential and Other Non-Occupational Environments**

**Estimated risk for non-occupational exposure is not of concern.**

PMV-01 is proposed for use in the greenhouse only. Consequently, it is unlikely that adults, youths and toddlers will be exposed to *Pepino mosaic virus*, strain CH2, isolate 1906. Even in the event of exposure, risk to the general population is not a concern since there were no signs that it caused any significant toxicity or disease in studies on laboratory animals and human cell cultures.

**Occupational Risks From Handling PMV-01**

**Occupational risks are not of concern when PMV-01 is used according to label directions, which include protective measures**

Workers handling PMV-01 can come into direct contact with *Pepino mosaic virus*, strain CH2, isolate 1906 on the skin, in the eyes, or by inhalation. For this reason, the product label will specify that workers must wear personal protective equipment, including waterproof gloves, long-sleeved shirts, long pants, a mist filtering respirator, eye goggles and shoes with socks. To minimize postapplication exposure, unprotected workers are restricted from entering areas treated with PMV-01 for 4 hours following application or until sprays have dried.

## Environmental Considerations

**What Happens When *Pepino mosaic virus*, strain CH2, isolate 1906 Is Introduced Into the Environment?**

**Environmental risks are not of concern.**

PMV-01 is proposed for use in greenhouse tomato and is not intended for outdoor uses. The greenhouse use of PMV-01 is not expected to result in sustained increases of *Pepino mosaic virus*, strain CH2, isolate 1906 in terrestrial and aquatic environments beyond natural background levels.

*Pepino mosaic virus*, strain CH2, isolate 1906 belongs to the genus *Potexvirus* in the family Alphaflexiviridae. The *Potexviruses* are exclusively plant pathogens with global distribution.

Contact with infected plants through tools, workers or, bumblebees is necessary for transmission to healthy plants. Infection of healthy plants occurs by contact to contaminated surfaces with damaged surfaces in the plant. The virus does not persist outside plant material and is inactivated by UV light.

Based on a critical review of an applicant-submitted aquatic plant study and information from public sources, no significant effects to birds, wild mammals, fish, terrestrial and aquatic non-target arthropods, terrestrial and aquatic non-arthropod invertebrates, or terrestrial and aquatic plants are expected when PMV-01 is applied according to directions on the label.

## Value Considerations

### What Is the Value of PMV-01?

**PMV-01 protects greenhouse tomatoes against the aggressive forms of the *Pepino Mosaic Virus*.**

PMV-01 provides protection against the *Pepino mosaic virus*, which causes a disease of greenhouse tomatoes that reduces crop yield and quality. There are no other products available to control this disease and growers rely on hygienic practices to exclude the virus and prevent infection of tomato plants. PMV-01 is compatible with current greenhouse tomato production practices.

## Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of the *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 (end-use product) to address the potential risks identified in this assessment are as follows.

### Key Risk-Reduction Measures

### Human Health

In the absence of an eye irritation study, *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 are considered eye irritants. In addition, all microorganisms, including *Pepino mosaic virus*, strain CH2, isolate 1906, contain substances that are potential sensitizers and thus, respiratory and dermal sensitivity may possibly develop in individuals exposed to potentially large quantities of *Pepino mosaic virus*, strain CH2, isolate 1906. In turn, workers handling or applying PMV-01 must wear waterproof gloves, long-sleeved shirts, long pants, eye goggles, a mist filtering respirator, and shoes with socks. Furthermore, all unprotected workers are restricted from entering treated areas during application and for 4 hours following application or until sprays have dried.

**Environment**

The end-use product label will include environmental precaution statements that limit contamination of aquatic systems from the use of PMV-01.

## Next Steps

Before making a final registration decision on *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

## Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01 (based on the Science Evaluation section of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

# Science Evaluation

## 1.0 The Active Substance, its Properties and Uses

### 1.1 Identity of the Active Ingredient

| | |
|---|---|
| **Active microorganism** | *Pepino mosaic virus*, strain CH2, isolate 1906 |
| **Function** | For the control of *Pepino mosaic virus* on greenhouse tomato |
| **Binomial name** | *Pepino mosaic virus*, strain CH2, isolate 1906 |
| **Taxonomic designation**[5] | |
| **Superkingdom** | Viruses |
| **Family** | Alphaflexiviridae |
| **Genus** | *Potexvirus* |
| **Species** | *Pepino mosaic virus* |
| **Strain** | CH2 |
| **Isolate** | 1906 |
| **Patent Status information** | No patent has been granted in Canada; there is also no patent pending. However, a patent has been granted in Belgium and Spain:-Belgium: Granted on 3 March 2017, Number BE1923391B1<br>-Spain: Granted on 21 March 2018, Number ES2603395B1<br>In the Netherlands the patent is pending:<br>-The Netherlands: Number NL2017307A |
| **Minimum purity of active** | *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient): minimum of $5 \times 10^5$ copies/µL<br>PMV-01 (end-use product): minimum of $5 \times 10^5$ copies/µL |
| **Identity of relevant impurities of toxicological, environmental and/or** | The technical grade active ingredient does not contain any impurities or micro contaminants known to be Toxic Substances Management Policy Track 1 substances. The |

[5] National Center for Biotechnology Information - Taxonomy Browser (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=112229)

| | |
|---|---|
| **significance.** | product must meet microbiological contaminants release standards. |

## 1.2 Physical and Chemical Properties of the Technical Grade Active Ingredient and the End-Use Products

**Technical Grade Active Ingredient – *Pepino mosaic virus*, strain CH2, isolate 1906**

| Property | Result |
|---|---|
| Colour | Dark green |
| Physical State | Liquid with some particles |
| Odour | Tomato leaves |
| Dynamic viscosity | 20°C ± 0.5°C : 64.3 cP to 4.4 cP; 40°C ± 0.5°C : 64.3 cP to 3.6 cP |
| pH | 5.89 |
| Density | 1.001–1.005 g/mL |

**End-use Product – PMV-01**

| Property | Result |
|---|---|
| Colour | Dark green |
| Physical State | Liquid with some particles |
| Odour | Tomato leaves |
| Dynamic viscosity | 20°C ± 0.5°C : 64.3 cP to 4.4 cP; 40°C ± 0.5°C : 64.3 cP to 3.6 cP |
| pH | 5.89 |
| Density | 1.001–1.005 g/mL |

## 1.3 Directions for Use

Apply one foliar application per crop cycle to greenhouse tomatoes at a rate of 4–8 L/ha. PMV-01 is to be applied on young tomato plants before the first cluster of flowers fully opens. Growers are required to obtain plant samples and send them to a designated laboratory to test for the presence of the *Pepino mosaic virus* prior to treatment with PMV-01. Only young tomato plants free of PepMV infection may be treated. Plant samples should also be collected after application of PMV-01 to confirm that the mild strain is present in the inoculated plants. Refer to the product label for additional instructions and conditions of use.

## 1.4 Mode of Action

PMV-01 protects tomato plants through cross-protection, which is based on similarity of nucleotide sequences and coat proteins between the mild and aggressive strains of PepMV. It is thought that the presence of the mild strain activates the plant's defense mechanism resulting in the inhibition of a subsequent infection by a related (aggressive) virus. Another explanation is based on the plant being able to recognize the viral coat proteins of a related aggressive) virus, preventing uncoating of the virus and subsequent replication of the virus particles. Cross-protection is considered effective when similarities in nucleotide sequence between PepMV strains is 90% or more.

## 2.0 Methods of Analysis

### 2.1 Methods for Identification of the Microorganisms

Acceptable methodologies for detection of the active ingredient, *Pepino mosaic virus*, strain CH2, isolate 1906, were submitted by the applicant. *Pepino mosaic virus*, strain CH2, isolate 1906 can be identified to the isolate level by nucleotide sequence determination.

### 2.2 Methods for Establishment of Purity of Seed Stock

Acceptable methods for establishment of purity of seed stock were fully described for the microbial pest control agent (MPCA). *Pepino mosaic virus*, strain CH2, isolate 1906 is preserved and maintained at -80°C. Back-up samples are stored at -20°C. The complete genome of *Pepino mosaic virus*, strain CH2, isolate 1906 was sequenced.

### 2.3 Methods to Define the Content of the Microorganism in the Manufactured Material Used for the Production of Formulated Products

The guarantees of the technical grade active ingredient and the end-use product are expressed in units of copies/µL. Representative data on five batches of end-use products, consisting of viral copy analysis, were submitted. The methods for potency testing and for determining the concentration of viral copies were adequately described.

### 2.4 Methods to Determine and Quantify Residues (Viable or Non-viable) of the Active Microorganism and Relevant Metabolites

As noted above, appropriate methods are available to enumerate viral copies and to distinguish this MPCA from other isolates of *Pepino mosaic virus*.

### 2.5 Methods for Determination of Relevant Impurities in the Manufactured Material

The quality assurance procedures used to limit contaminating microorganisms during the manufacture of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 are acceptable. These procedures include good hygienic practices for the maintenance, sanitation and cleaning of all laboratories and sterilization of all equipment used in the manufacturing process.

The absence of human pathogens and below-threshold levels of contaminating microorganisms were shown in the microbial screening of batches of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) by using standard methods for detecting and enumerating microbial contaminants of concern. In addition, all batches of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) must conform to the limits set out in the Organisation for Economic Co-operation and Development (OECD) issue paper on microbial contaminants for microbial pest control products [ENV/JM/MONO(2011)43].

### 2.6 Methods to Determine Storage Stability, Shelf-life of the Microorganism

Storage stability data were provided for PMV-01. Results support a storage period of 21 days at 4°C.

## 3.0 Impact on Human and Animal Health

### 3.1 Toxicity and Infectivity Summary

#### 3.1.1 Testing

The PMRA conducted a detailed review of the toxicological studies submitted in support of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01.

The studies submitted to fulfil the requirements for the health hazard assessment of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) included acute oral, inhalation and dermal studies. Additional reverse mutation assay testing and human cell line infectivity testing was performed.

In the acute oral toxicity study, 2 groups of 3 fasted, 9 week old CRL:(WI) female rats were given a single oral dose of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient; $5.0 \times 10^5$ copies/µL) in distilled water at doses of 2000 mg/kg body weight (bw). The animals were then observed for a period of up to 14 days with sacrifice on Day 14. There were no treatment related signs of toxicity observed in any animal.

In the acute dermal toxicity study, a group of young adult CRL:(WI) rats (5/sex) were dermally exposed to *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient; $5.0 \times 10^5$ copies/µL) at a dose of 2000 mg/kg bw for 24 hours to an area of approximately 10% of body surface area. Following exposure, the animals were observed for a period of 14 days. There were no treatment related signs of toxicity or skin irritation observed in any animal.

In the acute inhalation toxicity study, one group (5/sex) of 9 week old Wistar (Crl:WI) rats was exposed by the inhalation route to *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient; $5.0 \times 10^5$ copies/µL) for 4 hours to nose only at a concentration of 20.6 mg/L ± 2.0 mg/L (measured). Animals then were observed for 15 days. During exposure, shallow respiration was seen in all animals. After exposure, lethargy, hunched posture, laboured respiration, rales, piloerection and/or ptosis were observed among the treated animals between Days 1 and 4. In one male, the rales persisted until Day 8. There were no mortalities.

*Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient; $5.0 \times 10^5$ copies/µL) was evaluated for its potential to induce reverse mutations in five standard *Salmonella* Typhimurium strains (TA88, TA100, TA102, TA1535, and TA1537) in the absence and presence of a rat liver metabolic activation system (S9). Testing was conducted at several concentrations: 1.563, 31.25, 6.25, 12.5, 25, 50 and 100 µL/plate. No evidence of mutagenic activity was observed at any of the concentrations tested.

In an in vitro human cell line infectivity assay, 3 parallel groups of A549 cells were treated with 1.25% of *Pepino mosaic virus*, strain CH2, isolate 1906 ($5.0 \times 10^5$ copies/µL) in growth media for 24 hours. Treated cells were washed in a buffer solution; centrifuged and then re-cultured. This procedure was repeated 4 times. Viral copies were enumerated each time cells were washed and re-cultured. Because of the decrease in viral concentrations observed in each subsequent passage, it can be concluded that *Pepino mosaic virus*, strain CH2, isolate 1906 is not infective to human cell line A549 cells.

The end-use product requirement for a dermal irritation study was waived because no signs of dermal irritation were observed in the acute dermal toxicity study testing the technical grade active ingredient and the technical grade active ingredient is considered toxicologically equivalent to the end-use product.

Test results are summarized in Appendix I, Table 1.1.

### 3.1.2 Additional Information

A scientific rationale was provided to waive the technical grade active ingredient requirements for infectivity testing. The request to waive the technical grade active ingredient requirements for infectivity testing was supported by the lack of toxicity effects for strain CH2, isolate 1906 as well as published literature on the biological properties of plant viruses.

*Pepino mosaic virus* is a plant virus. Plant viruses are not related to any animal or human pathogens. Plant viruses are harmless to humans and other animals because they only reproduce in living plant cells. Moreover, plant viruses are ubiquitous in plants and fruits, and as a consequence they are continuously consumed by animals and humans. Cases of plant viruses causing diseases in humans have never been documented.

Plant viruses do not replicate outside of plant cells. The virus does not have a cellular structure and does not produce metabolites. The host range of the MPCA is mainly limited to Solanaceous plants. The MPCA does not have any known mechanism to cause adverse effects in human beings or other mammals.

A survey of published literature on the National Center for Biotechnology Information search engine performed by the PMRA using the keyword 'Pepino virus' has found no incidents, adverse or otherwise, involving the *Pepino mosaic virus* and humans or other mammals.

### 3.1.3 Incident Reports Related to Human and Animal Health

*Pepino mosaic virus*, strain CH2, isolate 1906 is a new active ingredient pending registration for use in Canada. Therefore, as of 2 February 2018, no incident reports were submitted to the PMRA.

### 3.1.4 Hazard Analysis

The database submitted by the applicant in support of registering *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01 was reviewed from the viewpoint of human health and safety and was determined to be sufficiently complete to permit a decision on registration.

Based on all the available information, the technical grade active ingredient, *Pepino mosaic virus*, strain CH2, isolate 1906 is of low toxicity by the oral, inhalation and dermal routes of exposure and is not a dermal irritant. The information also indicates that the MPCA is not infective or pathogenic. However, the MPCA is considered to be a potential sensitizer. Consequently, the hazard statement "POTENTIAL SENSITIZER" will appear on the principal display panel of the technical grade active ingredient. The statement "May cause sensitization. Avoid contact with skin and clothing. Avoid inhaling/breathing mist." is also required on the secondary panel of the label under the "PRECAUTIONS" section.

Similarly, the end-use product, PMV-01, is of low toxicity by the oral, pulmonary and dermal routes and is not a dermal irritant. As noted for the technical grade active ingredient, the end-use product is considered to be a potential sensitizer therefore the hazard statement "POTENTIAL SENSITIZER" will appear on the principal display panel of the end-use product label. The statement "May cause sensitization. Avoid contact with skin and clothing. Avoid inhaling/breathing mist." is also required on the secondary panel under the "PRECAUTIONS" section.

All microorganisms are considered to be mild ocular irritants and thus, the technical grade active ingredient and end-use product labels will include the signal words "CAUTION – EYE IRRITANT" and the precautionary statement "Avoid contact with eyes".

Higher tier subchronic and chronic toxicity studies were not required because the technical grade active ingredient was not acutely toxic by the oral, dermal or inhalation route of administration. Furthermore, no indications of infectivity or pathogenicity were observed in any the test animals treated with the technical grade active ingredient at Tier I.

Within the available scientific literature, there are no reports that suggest *Pepino mosaic virus*, strain CH2, isolate 1906 or other plant viruses have the potential to cause adverse effects on the endocrine system of animals. Based on the weight of evidence of available data, no adverse effects to the endocrine system are anticipated for this MPCA.

## 3.2 Occupational, Residential and Bystander Risk Assessment

### 3.2.1 Occupational Exposure and Risk

When handled according to the label instructions, the potential for dermal, eye and inhalation exposure for applicators, mixer/loaders, and handlers exists, with the primary exposure route being dermal. Since unbroken skin is a natural barrier to microbial invasion of the human body, dermal absorption could occur only if the skin were cut, if the microbe were a pathogen equipped with mechanisms for entry through or infection of the skin, or if metabolites were produced that

could be dermally absorbed. *Pepino mosaic virus*, strain CH2, isolate 1906 has not been identified as a dermal wound pathogen and does not contain any known toxic secondary metabolites. There is no indication that it could penetrate the intact skin of healthy individuals. Furthermore, toxicity testing with the technical grade active ingredient showed no signs of toxicity via the oral, inhalation or dermal routes of exposure. No evidence of skin irritation was noted in the submitted dermal toxicity studies. As an eye irritation study was not submitted, PMV-01 must be considered an eye irritant.

Also, the PMRA assumes that all microorganisms contain substances that can elicit positive hypersensitivity reactions, regardless of the outcome of sensitization testing.

Risk mitigation measures such as personal protective equipment, including waterproof gloves, eye goggles, long-sleeved shirts, long pants, a NIOSH-approved particulate filtering facepiece respirator with any N, R, or P filter, and socks with shoes are required to minimize exposure and protect applicators, mixer/loaders and handlers that are likely to be exposed. In addition, all unprotected workers and users are prohibited from entering treated areas where PMV-01 has been applied for 4 hours or until the sprays have dried.

Label warnings, restrictions and risk mitigation measures are adequate to protect users of PMV-01 and no significant occupational risks are anticipated from these products.

### 3.2.2 Residential and Bystander Exposure and Risk

Overall, the PMRA does not expect that residential and bystander exposures will pose a health risk of concern on the basis of the low toxicity profile for PMV-01, the low infectivity/pathogenicity profile for *Pepino mosaic virus*, strain CH2, isolate 1906, the expectation that the label will be followed by commercial applicators in the use of PMV-01, and that PMV-01 is only applied inside commercial greenhouses. As well, *Pepino mosaic virus* is a common viral disease in commercially grown tomatoes and the use of PMV-01 is not expected to cause sustained increases in exposure to bystanders beyond natural levels. Consequently, the health risk to infants and children is not expected to be of concern.

## 3.3 Dietary Exposure and Risk Assessment

### 3.3.1 Food

While the proposed use pattern may result in dietary exposure with possible residue in or on agricultural commodities, dietary risk is not expected to be of concern for the general population and sensitive subpopulations such as infants and children, or to animals because *Pepino mosaic virus*, strain CH2, isolate 1906 demonstrated no pathogenicity, infectivity or toxicity in acute oral toxicity and tissue culture studies. Furthermore, higher tier subchronic and chronic dietary exposure studies were not required because of the low toxicity and lack of infectivity or pathogenicity associated with the MPCA.

### 3.3.2 Drinking Water

Health risks are not expected from exposure to *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) via drinking water because exposure will be low from operational applications and there were no harmful effects observed in acute oral toxicity testing and tissue culture studies. The label for PMV-01 instructs users not to contaminate irrigation or drinking water supplies or aquatic habitats through equipment cleaning or waste disposal. Aerial application is also prohibited. Furthermore, municipal treatment of drinking water is expected to reduce the transfer of residues to drinking water.

### 3.3.3 Acute and Chronic Dietary Risks for Sensitive Subpopulations

Calculations of acute reference doses (ARfDs) and acceptable daily intakes (ADIs) are not usually possible for predicting acute and long term effects of microbial agents in the general population or to potentially sensitive subpopulations, particularly infants and children. The single (maximum hazard) dose approach to testing MPCAs is sufficient for conducting a reasonable general assessment of risk if no significant adverse effects are noted in acute toxicity and infectivity tests. Based on all the available information and hazard data, the PMRA concludes that *Pepino mosaic virus*, strain CH2, isolate 1906 is of low toxicity, is not pathogenic or infective to mammals, and that infants and children are likely to be no more sensitive to the MPCA than the general population. Thus, there are no threshold effects of concern and, as a result, there is no need to require definitive (multiple dose) testing or apply uncertainty factors to account for intra- and interspecies variability, safety factors or margins of exposure. Further factoring of consumption patterns among infants and children, special susceptibility in these subpopulations to the effects of the MPCA, including neurological effects from pre- or post-natal exposures, and cumulative effects on infants and children of the MPCA and other registered microorganisms that have a common mechanism of toxicity, does not apply to this MPCA. As a result, the PMRA has not used a margin of exposure (safety) approach to assess the risks of *Pepino mosaic virus*, strain CH2, isolate 1906 to human health.

### 3.3.4 Aggregate Exposure and Risk

Based on the toxicity and infectivity test data submitted and other relevant information in the PMRA's files, there is reasonable certainty that no harm will result from aggregate exposure of residues of *Pepino mosaic virus*, strain CH2, isolate 1906 to the general Canadian population, including infants and children, when the end-use product is used as labelled. This includes all anticipated dietary (food and drinking water) exposures and all other non-occupational exposures (dermal and inhalation) for which there is reliable information. Dermal and inhalation exposure to the general public will be low since the product is not allowed for use on turf, residential or recreational areas. Furthermore, adverse effects from exposure to other *Pepino mosaic virus* encountered in the environment have not been reported. Even if there is an increase in exposure to this active ingredient from the use of PMV-01, there should not be any increase in potential human health risk.

### 3.3.5 Maximum Residue Limits

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to

remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally specified as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada specifies science-based MRLs to ensure the food Canadians eat is safe.

Residues of *Pepino mosaic virus*, strain CH2, isolate 1906 on treated food crops, at the time of harvest, are anticipated following foliar applications to agricultural crops. Consequently, the PMRA has applied a hazard-based approach for determining whether an MRL is required for this microorganism. The risks anticipated for dietary exposure are considered low as no adverse effects from dietary exposure have been attributed to natural populations of *Pepino mosaic virus*, and no adverse effects were observed in the acute oral toxicity and tissue culture studies. In addition, the likelihood of residues contaminating drinking water supplies is negligible to non-existent. Therefore, the PMRA has determined that specification of an MRL under the PCPA is not required for *Pepino mosaic virus*, strain CH2, isolate 1906.

### 3.4 Cumulative Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. In its assessment of common mechanism of toxicity, PMRA considers both the taxonomy of MPCAs and the production of any potentially toxic metabolites. For the current evaluation, the PMRA did not identify information indicating that *Pepino mosaic virus*, strain CH2, isolate 1906 shares a common mechanism of toxicity with other registered MPCAs. Therefore there is no requirement for a cumulative health risk assessment at this time.

## 4.0 Impact on the Environment

### 4.1 Fate and Behaviour in the Environment

Environmental fate data (Tier II/III) are not normally required at Tier I, and are only triggered if significant toxicological effects in non-target organisms are noted in Tier I testing.

*Pepino mosaic virus*, strain CH2, isolate 1906 belongs to the genus *Potexvirus* in the family Alphaflexiviridae. The *Potexviruses* are exclusive plant pathogens with global distribution. Contact with infected plants through tools, workers, bumblebees is necessary for transmission to healthy plants. Infection of healthy plants occurs by contact to contaminated surfaces with damaged surfaces in the plant. The virus does not persist outside plant material and is inactivated by UV light. Since the virus is inactivated by UV light, virus particles in aerosols that might be formed during spraying and subsequently escape the greenhouse, will be deactivated rapidly.

The persistence and mobility of *Pepino mosaic* virus, strain CH2, isolate 1906 in soil was investigated in one laboratory experiment and in one greenhouse experiment. In the laboratory experiment at 4°C and 20°C, a stable viral concentration was observed over a period of 14 days followed by a steady decline. The virus remained present up to a period of 31 days (at 20°C) and

up 52 days (at 4°C). Samples obtained from greenhouse tomatoes treated with PMV-01 revealed that no viral particles are detectable after eight months.

A study was performed to assess the persistence of *Pepino mosaic* virus, strain CH2, isolate 1906 in water. This study concluded that levels of *Pepino mosaic* virus, strain CH2, isolate 1906 in water will return to naturally occurring background levels within a year even at an applied concentration that was 7 orders of magnitude higher than expected under normal use of PMV-01.

Overall, it is not expected that the greenhouse use of PMV-01 will result in sustained increases of *Pepino mosaic* virus, strain CH2, isolate 1906 in outdoor terrestrial and aquatic environments beyond naturally occurring background levels.

### 4.2 Effects on Non-Target Species

The PMRA has a four tiered approach to environmental testing of microbial pesticides. Tier I studies consist of acute studies on up to seven broad taxonomic groups of non-target organisms exposed to a maximum hazard or Maximum Challenge Concentration (MCC) of the MPCA. The MCC is generally derived from the amount of the MPCA, or its toxin, expected to be available following application at the maximum recommended label rate multiplied by a safety factor. Tier II studies consist of environmental fate (persistence and dispersal) studies as well as additional acute toxicity testing of MPCAs. Tier III studies consist of chronic toxicity studies (life cycle studies), as well as definitive toxicity testing (for example, $LC_{50}$, $LD_{50}$). Tier IV studies consist of experimental field studies on toxicity and fate, and are required to determine whether adverse effects are realized under actual use conditions.

The type of environmental risk assessment conducted on MPCAs varies depending on the tier level that was triggered during testing. For many MPCAs, Tier I studies are sufficient to conduct environmental risk assessments. Tier I studies are designed to represent "worst-case" scenarios where the exposure conditions greatly exceed the expected environmental concentrations. The absence of adverse effects in Tier I studies are interpreted as minimal risk to the group of non-target organisms. However, higher tiered studies will be triggered if significant adverse effects on non-target organisms are identified in Tier I studies. These studies provide additional information that allows the PMRA to refine the environmental risk assessments. In the absence of adequate environmental fate and/or field studies, a screening level risk assessment can be performed to determine if the MPCA is likely to pose a risk to a group of non-target organisms.

The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ=exposure/toxicity), and the risk quotient is then compared to the level of concern.

If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (environmental fate and/or field testing results). Refinements to the risk assessment

may continue until the risk is adequately characterized or no further refinements are possible.

### 4.2.1 Effects on Terrestrial Organisms

Acceptable scientific rationales based on published scientific literature were submitted in lieu of Tier I testing requirements on non-target birds, wild mammals, terrestrial arthropods, terrestrial non-arthropod invertebrates, terrestrial plants and microorganisms.

The rationales were based on the following:

- *Pepino mosaic virus*, strain CH2, isolate 1906 is a naturally occurring plant virus strain. Its host plants are mainly from the Solanaceae family. *Pepino mosaic virus* infection and replication is known to be very specific to plants and has not been reported to occur in other organisms, including humans or animals.
- Some weed species have been reported to harbour the virus, although results of different studies are conflicting. There is no identified risk associated with these weed species, other than their potential to act as sources of infection for tomato crops if infected weeds grow in close proximity to tomato crops.
- PMV-01 is a plant virus that is applied to tomato plants in greenhouses. In greenhouse tomato cultures the release of *Pepino mosaic virus*, strain CH2, isolate 1906 to the environment through air or soil is very limited. The virus does not persist outside plant materials and it does not replicate in animals. The virus is inactivated by UV light.

Based on all the available data and information on the effects of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) to terrestrial non-target organisms, there is reasonable certainty that no harm will be caused to birds, wild mammals, arthropods, non-arthropod invertebrates, plants or to other non-target microorganisms from the use of PMV-01 in greenhouse tomato crops.

### 4.2.2 Effects on Aquatic Organisms

Acceptable scientific rationales based on published scientific literature were submitted in lieu of Tier I testing requirements on freshwater fish, aquatic arthropods, and aquatic plants.

The rationales were based on the following:

- *Pepino mosaic virus*, strain CH2, isolate 1906 is a naturally occurring plant virus strain. Its host plants are mainly from the Solanaceae family. *Pepino mosaic virus* infection and replication is known to be very specific to plants and has not been reported to occur in other organisms, including humans or animals.
- PMV-01 is a plant virus that is applied to tomato plants in greenhouses. This use pattern would not result in significant exposure to aquatic organisms such as fish. In greenhouse tomato cultures the release of *Pepino mosaic virus*, strain CH2, isolate 1906 to the environment is very limited. While *Pepino mosaic virus* can be transmitted through recirculation of drainage water, the transmission efficiency is limited.

- The virus does not persist outside plant material and it does not replicate in animals.

In addition to the above scientific rationales, a study was submitted on the hazards of this MPCA to freshwater plants. In this study, duckweed (*Lemna minor*) were exposed to *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient; $5.0 \times 10^5$ copies/µL) at a nominal concentration of 1000 mg/L under static conditions. The growth rate (as measured by final frond number, wet weight and dry weight) was not inhibited by the treatment.

Based on all the available data and information on the effects of *Pepino mosaic virus*, strain CH2, isolate 1906 to aquatic non-target organisms, there is reasonable certainty that no harm will be caused to fish, aquatic arthropods, aquatic non-arthropod invertebrates or aquatic plants from the use of PMV-01 in greenhouse tomato crops. As a precaution, standard label statements will prohibit handlers from contaminating aquatic habitats.

Test results are summarized in Appendix I, Table 1.2.

### 4.3 Incident Reports Related to the Environment

*Pepino mosaic virus*, strain CH2, isolate 1906 is a new active ingredient pending registration for use in Canada. Therefore, as of 2 February 2018, no incident reports were submitted to the PMRA.

## 5.0 Value

The applicant provided results of efficacy trials, use history, scientific rationales, published information and benefit information to support the value assessment. One application of PMV-01 is applied to young tomato plants that are free of PepMV infection.

The aggressive *Pepino mosaic virus* strains present in Canada are CH2, EU and US1. In lieu of trials using specific aggressive Canadian PepMV strains, the applicant provided studies using European isolates of the same strains as those found in Canada. This was acceptable because the similarity of aggressive European and Canadian PepMV strains is high. Results of the efficacy trials demonstrated that the rate of 4–8 L/ha is appropriate to prevent PepMV infection. The high rate should be used when faster colonization of plants is required. The trials demonstrated that PMV-01 is effective against the aggressive strains CH2, EU, and US1. The efficacy of PMV-01 on the LP strain was extrapolated from trial results involving the EU strain because they have very similar nucleotide sequences. Use history information from various countries in Europe and North Africa showed that PMV-01 is efficacious against the aggressive CH2 and EU strains in a variety of greenhouse conditions. No phytotoxic effects of PMV-01 have been observed in any of the trials or in operational scale use of this product in Europe.

There are no other products registered in Canada to manage PepMV in greenhouse tomatoes. The growers rely on disinfection of the greenhouse to lower the chances of spreading the virus. The disease has spread across Canada and a PepMV management strategy is a priority for Canadian greenhouse tomato producers. Thus, this product will provide Canadian growers with the first in-crop option to manage this important disease.

## 6.0 Pest Control Product Policy Considerations

### 6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, in other words, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

*Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 were assessed in accordance with the PMRA Regulatory Directive DIR99-03.[6]

- *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) does not meet the Track 1 criteria because the active ingredient is a biological organism and hence is not subject to the criteria used to define persistence, bio-accumulation and toxicity properties of chemical control products.

- There are also no formulants, contaminants or impurities present in the end-use product that would meet the TSMP Track-1 criteria.

### 6.2 Formulants and Contaminants of Health Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[7] The list is used as described in the PMRA Notice of Intent NOI2005-01[8] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[9] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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6 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy.*

7 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-11-30) pages 2641-2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613: *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

8 Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

9 Regulatory Directive DIR2006-02, *PMRA Formulants Policy.*

- The technical grade active ingredient, *Pepino mosaic virus*, strain CH2, isolate 1906, does not contain formulants of health or environmental concern as identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641-2643: *List of Pest Control Product Formulants of Health or Environmental Concern*.

- The end-use product, PMV-01, does not contain formulants of health or environmental concern as identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641-2643: *List of Pest Control Product Formulants of Health or Environmental Concern*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and DIR2006–02.

## 7.0 Summary

### 7.1 Methods for Analysis of the Microorganism as Manufactured

The product characterization data for *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 were judged to be adequate to assess their potential human health and environmental risks. The technical grade active ingredient was characterized and the specifications of the end-use product were supported by the analyses of a sufficient number of batches. All batches of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) must conform to the limits set out in the OECD issue paper on microbial contaminants for microbial pest control products [ENV/JM/MONO(2011)43]. Storage stability data support storage at 4°C for up to 21 days for PMV-01.

### 7.2 Human Health and Safety

The scientific waiver rationales, acute toxicity and human cell line infectivity studies submitted in support of *Pepino mosaic virus*, strain CH2, isolate 1906 were determined to be sufficiently complete to permit a decision on the registration of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 (end-use products). Based on all the available information, the technical grade active ingredient, *Pepino mosaic virus*, strain CH2, isolate 1906, is of low toxicity and not infective or pathogenic by the oral, inhalation, and dermal routes of exposure. This information also indicates that PMV-01 will not be irritating to the skin. *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01, however, are considered as eye irritants and thus, the signal words "CAUTION – EYE IRRITANT" must appear on the principal display panel of the labels. Since *Pepino mosaic virus*, strain CH2, isolate 1906 is also considered to be a potential sensitizer, the signal words "POTENTIAL SENSITIZER" are required on the principal display panels of the end-use product and technical grade active ingredient.

When handled according to prescribed label instructions, the potential for dermal, eye and inhalation exposure for mixer/loaders, applicators, and handlers exists, with the primary source of exposure to workers being dermal. Respiratory and dermal sensitivity could possibly develop upon repeated exposure to the product since all microorganisms, including *Pepino mosaic virus*,

strain CH2, isolate 1906, contain substances that are potential sensitizers. Therefore, anyone handling or applying PMV-01 must wear waterproof gloves, eye goggles, a long-sleeved shirt, long pants, NIOSH-approved particulate filtering facepiece respirator with any N, R, or P filter, and shoes with socks. In addition, to minimize postapplication exposure, all unprotected workers are restricted from entering areas treated with PMV-01 for 4 hours or until sprays have dried.

The health risk to the general population, including infants and children, as a result of bystander exposure and/or chronic dietary exposure is not of concern due to the low toxicity/pathogenicity profile for *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient) and PMV-01 as well as the absence of sustained increases in exposure to bystanders beyond natural levels. The specification of an MRL under the *Pest Control Products Act* is not required for *Pepino mosaic virus*, strain CH2, isolate 1906.

### 7.3 Environmental Risk

The scientific studies, rationales and supporting published scientific literature in support of *Pepino mosaic virus*, strain CH2, isolate 1906 (technical grade active ingredient), and its associated end-use product, PMV-01, were determined to be sufficiently complete to permit a decision on registration. The greenhouse use of PMV-01 containing *Pepino mosaic virus*, strain CH2, isolate 1906, is not expected to pose a risk to non-target organisms when the directions for use on the label are followed. The proposed greenhouse use of PMV-01 on tomato is not expected to result in sustained increases of *Pepino mosaic virus*, strain CH2, isolate 1906, in terrestrial and aquatic environments.

As a general precaution, the product label will direct handlers to not contaminate surface water by disposal of equipment wash waters.

### 7.4 Value

The results of efficacy trials, use history information from Europe and North Africa as well as published information provided by the applicant have demonstrated that PMV-01 is an effective product for the protection of greenhouse tomatoes against the aggressive strains of PepMV.

## 8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing registration for the sale and use of *Pepino mosaic virus*, strain CH2, isolate 1906 and PMV-01, containing the technical grade active ingredient *Pepino mosaic virus*, strain CH2, isolate 1906, to protect greenhouse tomatoes against *Pepino mosaic virus*.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the values of the pest control products are acceptable

## List of Abbreviations

| | |
|---|---|
| °C | degree(s) Celsius |
| µL | microlitre |
| ADI | acceptable daily intake |
| ARfD | acute reference dose |
| bw | body weight |
| cP | centipoise |
| DNA | deoxyribonucleic acid |
| $EC_{50}$ | effective concentration on 50% of the population |
| g | gram |
| ha | hectare(s) |
| kg | kilogram |
| L | litre |
| $LC_{50}$ | lethal concentration 50% |
| $LD_{50}$ | lethal dose 50% |
| mg | milligram |
| mL | millilitre |
| MPCA | microbial pest control agent |
| MRL | maximum residue limit |
| NIOSH | National Institute for Occupational Safety and Health |
| OECD | Organization for Economic Co-operation and Development |
| PMRA | Pest Management Regulatory Agency |
| PepMV | *Pepino mosaic virus* |
| RQ | risk quotient |
| TGAI | technical grade of the active ingredient |
| TSMP | Toxic Substances Management Policy |
| UV | ultraviolet |

# Appendix I Tables and Figures

## Table 1.1 Toxicity profile of *Pepino mosaic virus*, strain CH2, isolate 1906 and its associated End-use Product, PMV-01

| Study Type/Animal/PMRA# | Study Results |
|---|---|
| 14-Day Acute Oral Toxicity<br><br>Wistar Rat<br><br>PMRA #2747733 | There were no mortalities.<br><br>There were no treatment related clinical signs, no abnormal necropsy findings and no differences in body weight gain between groups.<br><br>The technical grade active ingredient was of low toxicity. The oral $LD_{50}$ > 2000 mg/kg bw in female rats. |
| 14-Day Acute Dermal Toxicity<br><br>Wistar Rat<br><br>PMRA #2747801 | There were no mortalities.<br><br>There were no treatment related clinical signs, no abnormal necropsy findings and no differences in body weight gain between groups.<br><br>The technical grade active ingredient was of low toxicity and no signs of irritation were observed. The dermal $LD_{50}$ > 2000 mg/kg bw in male and female rats. |
| 15-Day Acute Inhalation Toxicity<br><br>Wistar Rat<br><br>PMRA #2747783<br>PMRA #2747784<br>PMRA #2747785 | There were no mortalities.<br><br>During exposure, shallow respiration was seen in all animals. After exposure, lethargy, hunched posture, laboured respiration, rales, piloerection and/or ptosis were seen among the animals between Days 1 and 4. In one male, the rales persisted until Day 8.<br><br>The technical grade active ingredient was of low toxicity. The inhalation $LC_{50}$ > 20.6 mg/l. in male and female rats. |
| Tissue Culture – Infectivity<br><br>Human A549 cells<br><br>PMRA #2747766 | Viral copies decreased with each subsequent re-culture and enumeration.<br><br>The technical grade active ingredient was not infective to Human A549 cells. |
| Reverse mutation assay<br><br>*Salmonella* Typhimurium strains TA88, TA100, TA102, TA1535, and TA1537 w and w/o S9 activation<br><br>PMRA #2747795<br>PMRA #2747795 | Mutagenic activity was not observed. |

**Table 1.2 Toxicity of *Pepino mosaic virus*, strain CH2, isolate 1906 to Non-Target Species**

| Study Type/Animal/PMRA # | Study Results |
|---|---|
| 7-Day Growth Inhibition<br><br>Duckweed<br><br>PMRA #2747799 | The growth rate (as measured by final frond number, wet weight and dry weight) was not inhibited in the test group.<br><br>The technical grade active ingredient was of low toxicity. The aquatic $EC_{50}$ > 1000 mg/L. |

**Table 2 List of Supported Uses**

Pest: *Pepino mosaic virus* (PepMV), strains CH2, EU, LP and US1

Crop: Greenhouse tomato

Application rate: 4–8 L/ha

Number of applications: one per cycle

Application timing: PMV-01 is to be applied on young tomato plants before the first cluster of flowers fully open.

Other instructions:

Collect plant samples and submit them for laboratory analysis prior to application of PMV-01.

Only young tomato plants free of PepMV infection may be treated.

# References

## 1.0 The active substance, its properties and uses


| PMRA Document Number | Reference |
|---|---|
| 2747693 | 2017, PMRA Canada Application: TGAI: *Pepino mosaic virus*, strain CH2, isolate 1906 EUP: PMV(R)-01, DACO: M2.1, M2.10,M2.10.1, M2.10.2, M2.10.3, M2.11, M2.12, M2.13, M2.14, M2.2, M2.3, M2.4, M2.5, M2.6, M2.7, M2.7.1, M2.7.2, M2.7.3, M2.8, M2.9, M2.9.1, M2.9.2, M2.9.3 |
| 2747694 | 2017, Confidential Business Information Reference Document for PMRA Canada Application: TGAI: *Pepino mosaic virus*, strain CH2, isolate 1906 EUP: PMV(R)-01, DACO: M2.1, M2.10, M2.10.1, M2.10.2, M2.10.3, M2.11, M2.12, M2.13, M2.14, M2.2, M2.3, M2.4, M2.5, M2.6, M2.7, M2.7.1, M2.7.2, M2.7.3, M2.8, M2.9, M2.9.1, M2.9.2, M2.9.3, CBI |
| 2747695 | 2002, Complete sequence of the *Pepino mosaic virus* RNA genome, DACO: M2.7.1, M2.7.2, M2.8 |
| 2747696 | 2012, *Pepino mosaic virus* (PepMV) : Hazards when used as microbial pesticide (Revised version of the edition from 2011 that was included in the original Annex II dossier submitted to the Rapporteur Member State end of July 2012, DACO: M2.7.2, M2.8, CBI |
| 2747697 | 2004, New natural hosts of *Pepino mosaic virus* in Spain, DACO: M2.7.2 |
| 2747698 | 2002, Complete nucleotide sequence of the genomic RNA of a French isolate of *Pepino mosaic virus* (PepMV), DACO: M2.7.1, M2.7.2, M2.8 |
| 2747700 | 2009, Basil (*Ocimum basilicum*), a new host of *Pepino mosaic virus*, DACO: M2.7.2 |
| 2747702 | 2012, Physical and chemical properties and low temperature storage stability of PMV-01, DACO: M2.12, CBI |
| 2747704 | 2001, Management of *Pepino mosaic virus* in Greenhouse Tomatoes, DACO: M2.7.2 |
| 2747705 | 2000, *Pepino mosaic*, a new disease of tomatoes, DACO: M2.7.2 |
| 2747706 | 2001, First Report of *Pepino mosaic virus* in Canada and the United States, DACO: M2.7.2 |
| 2747707 | 2006, Cross protection, DACO: M2.7.2 |
| 2747709 | 2006, Introduction to Plant Viruses, the Invisible Foe, DACO: M2.7.2 |
| 2747710 | 2009, Mixed Infections of *Pepino mosaic virus* strains Modulate the Evolutionary Dynamics of this Emergent Virus, DACO: M2.7.2 |
| 2747711 | 2009, Real-time quantitative PCR based sensitive detection and genotype discrimination of *Pepino mosaic virus*, DACO: M2.7.1, M2.8, M2.9.2 |
| 2747712 | 2012, PMV-01: Storage stability study 2: Tomato watery leaf extract containing PepMV, strain CH2, isolate 1906, DACO: M2.10.2, M2.11, M2.12, M2.7.2, CBI |
| 2747713 | 2012, PMV-01: Storage stability study 2: Tomato watery leaf extract containing PepMV, strain CH2, isolate 1906, DACO: M2.10.2, M2.11, M2.12, CBI |
| 2747714 | 2011, Storage stability study: Tomato watery leaf extract containing PepMV, strain CH2, isolate 1906, DACO: M2.10.2, M2.11, M2.12, CBI |
| 2747715 | 2011, Storage stability study : Tomato watery leaf extract containing PepMV, strain |

CH2, isolate 1906, DACO: M2.10.2, M2.11, M2.12, CBI

2747716 2012, Study on alternative, non-tomato host plants of *Pepino mosaic virus*, DACO: M2.7.1, M2.7.2, CBI

2747717 2012, Tomato watery leaf extract containing PepMV, strain CH2, isolate 1906, Study on genetic stability of viral isolate 1906, DACO: M2.7.2, M2.8, CBI

2747718 2010, *Pepino mosaic virus*: a successful pathogen that rapidly evolved from emerging to endemic in tomato crops, DACO: M2.7.1, M2.7.2, M2.8

2747719 2010, Cross-protection or enhanced symptom display in greenhouse tomato co-infected with different *Pepino mosaic virus* isolates, DACO: M2.7.2

2747720 2011, Differential Tomato Transcriptomic Responses Induced by *Pepino mosaic virus* Isolates with Differential Aggressiveness., DACO: M2.7.2

2747722 2008, Genetic characterization of *Pepino mosaic virus* isolates from Belgian greenhouse tomatoes reveals genetic recombination, DACO: M2.7.2

2747723 2009, *Pepino mosaic virus* isolates and differential symptomatology in tomato, DACO: M2.7.1, M2.7.2

2747724 2009, Seed transmission of *Pepino mosaic virus* in tomato, DACO: M2.7.1

2747725 2008, Complete genomic RNA sequence of the Polish *Pepino mosaic virus* isolate belonging to the US2 strain, DACO: M2.7.1, M2.7.2

2747726 2013, Ratio of mutated versus wild-type coat protein sequences in *Pepino mosaic virus* determines the nature and severity of yellowing symptoms on tomato plants, DACO: M2.7.2

2747727 2010, Evidence for RNA recombination between distinct isolates of *Pepino mosaic virus*, DACO: M2.7.2

2747729 2009, New necrotic isolates of *Pepino mosaic virus* representing the CH2 genotype, DACO: M2.7.1, M2.7.2

2747730 2011, Single mutation converts mild pathotype of the *Pepino mosaic virus* into necrotic one, DACO: M2.7.2, M2.8

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## 2.0 Impact on human and mammalian animal health

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## 3.0 Impact on the environment

**PMRA Document Number** **Reference**


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## 4.0 Value

**PMRA Document Number** **Reference**


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